REMARKS/ARGUMENTS

Claims 1 – 5, 7, 13, 15 – 19, and 22 – 30 are pending in this application. Claims 6 and 14 were previously cancelled and claims 8 – 12, 20 and 21 were previously withdrawn. Claims 1 – 5, 7, 13, 15 – 19, and 22 – 30 stand rejected.

I. Rejection Under 35 U.S.C. § 112, first paragraph – Enablement Rejection.

Claims 1-5, 7, 13, 15-19 and 22-30 stand rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. Applicants respectfully traverse this rejection for at least the reasons as set forth below.

It is settled law that a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enablement requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein. MPEP 2164.04 citing *In re Marzocchi*, 58 C.C.P.A. 1069, 439 F.2d 220, 223, 169 U.S.P.Q. (BNA) 367, 369 (CCPA 1971). Thus, the PTO has the initial burden of challenging a presumptively correct assertion of enablement in the disclosure. Only after the PTO provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility does the burden shift to the applicant to provide rebuttal evidence sufficient to convince such a person of the invention's asserted utility. *See In re Bundy*, 642 F.2d 430, 433, 209 U.S.P.Q. (BNA) 48, 51 (CCPA 1981).

The PTO has not provided any credible evidence showing that one of ordinary skill in the art would ***reasonably doubt*** the asserted utility of the claimed invention and has therefore not met its initial burden.

The Examiner has alleged for various reasons that the instant claims are not enabled by the present disclosure. In particular, the Examiner purports that the state of the art would require undue experimentation for administering peptides to induce immune tolerance to prevent/delay the onset of Type 1 diabetes in humans because such methods were unpredictable at the time of the present invention. The Examiner's alleged reasons for lack of enablement will be addressed and shown to fail to provide a *prima facie* case of non-enablement.

A. No *Prima Facie* Case of Lack of Enablement has been Established.

i. Post-filing date references should not be used in an enablement rejection.

MPEP 2164.05(a) and In re Hogan (559 F.2d 595, 605, 194 USPQ 527, 537 (CCPA 1977)) make clear that post-filing date references should not be used to demonstrate that the patent is non-enabling. An exception to this rule exists if a later-dated reference provides evidence of what one skilled in the art would have known **on or before** the effective filing date of the patent application. *In re Hogan*, 559 F.2d 595, 605, 194 USPQ 527, 537 (CCPA 1977).

The references being relied on by the Examiner (after reopening prosecution) for lack of enablement are as follows:

1) Marketletter (1999);

2) Pozzilli (2000);

3) Dong (1999);

4) WO 02/053092 (July 2002)

5) Kraus and Mayer (2005);

6) Skylar (2005)

7) Bell (2008);

8) von Herrath and Nepom (2009);

9) Van der Worp (2010) and

10) Leslie (2010).

Marketletter, Pozzilli and Dong were relied on in the prior enablement rejection. References 4 – 10 are newly relied on by the examiner in this office action. As an initial matter, each of references 4 – 10 were published **after** the priority date of the present application. None of these references are being relied on for what one skilled in the art would have known **on or before** the effective filing date of the patent application. Rather, each of these references are being relied on for what they disclose as of their respective publication dates. As such, these references should not be used in an enablement rejection.

ii. Pre-filing date references do not establish a *prima facie* case of lack of enablement.

As has been extensively discussed in the record, none of the pre-filing date references establish a *prima facie* case of lack of enablement. It is settled law that a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enablement requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein. MPEP 2164.04 citing *In re Marzocchi*, 58 C.C.P.A. 1069, 439 F.2d 220, 223, 169 U.S.P.Q. (BNA) 367, 369 (CCPA 1971). Thus, the PTO has the initial burden of challenging a presumptively correct assertion of enablement in the disclosure. Only after the PTO provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility does the burden shift to the applicant to provide rebuttal evidence sufficient to convince such a person of the invention's asserted utility. *See In re Bundy*, 642 F.2d 430, 433, 209 U.S.P.Q. (BNA) 48, 51 (CCPA 1981).

The PTO has not provided any credible evidence showing that one of ordinary skill in the art would ***reasonably doubt*** the asserted utility of the claimed invention and has therefore not met its initial burden.

The first pre-filing date reference relied on—Marketletter Pubs (UK) 13 September 1999 ("*Marketletter*")—deals with two unsubstituted peptides, which are much different than the claimed Ig-GAD2 fusion protein, tested in Multiple Sclerosis and Rheumatoid Arthritis, which are different autoimmune disorders having different initiating autoantigens and different etiologies as compared with Type 1 diabetes.

The second reference, Pozzilli, P. et. al, Diabetologi (2000) 43:1000-1004, deals with the effects of oral insulin on residual beta cell function. Again, a completely different therapeutic agent than presently claimed.

Finally, the third pre-filing date reference, Dong, V.M. *et al.*, Ped. Transplan. 1999; 3:181-192 ("*Dong*"), is merely a general review of tissue graft transplant tolerance (unrelated to treatment of any autoimmune disorder let alone Type 1 diabetes) and contains nothing to call in to question use of any fusion protein construct for delaying or preventing Type 1 diabetes. At

most, these references are only tangentially related to the presently claimed invention and simply do not cast any doubt, let alone any reasonable doubt, on the presently clamed invention which entails an altogether different therapeutic agent and altogether different disease state than those discussed in the references relied upon by the PTO. This is simply not enough to establish a *prima facie* case of lack of enablement.

Additionally, even if these reference were prior art, which is not admitted, none of them disclose anything to call into question the presently claimed soluble fusion protein construct. Rather, these references each deal with completely different therapeutic modalities.

Furthermore, Applicants point out that the specification provides substantial guidance as to how to practice the presently claimed invention. For example:

- Guidance as to how to make the constructs used in the claimed methods is provided at pages 45, line 13 – page 47, line 3;
- General dosing guidance is provided at page 34, line 21- page 37, line 17;
- Guidance on how to determine whether administration of a claimed fusion protein effectively prevented or delayed diabetes in humans or mice is provided at page 42, line 3 – page 42, line 7 and page 45, lines 5 – 11; and
- Guidance on how to determine if a subject has undergone insulin autoantibody seroconversion is provided at page 55, line 15 – page 56, line 24.

For at least the foregoing reasons, no *prima facie* case of lack of enablement has been established. Reversal of this rejection is therefore respectfully requested.

B. Even assuming, *arguendo,* that a *prima facie* case exists, Applicants previously rebutted it.

To further demonstrate that Applicants' claimed invention was enabled at the time of filing, Applicants previously submitted a declaration under 37 CFR 1.312 showing that the claimed method effectively prevents and/or delays the onset of Type 1 diabetes in the gold standard NOD mouse model for that disease. ("Zaghouani Declaration"). As has been clearly established in the record, the NOD mouse model used in the experiment described in the Zaghouani Declaration is considered the gold standard animal model for Type 1 diabetes, regardless of whether some unrelated agent in the past has shown efficacy in that model that did not translate to humans. The pharmaceutical industry is replete with molecules that showed

efficacy in gold standard models that failed to achieve FDA approval—this does not render later, different candidate molecules unpatentable.

It was clear error to reject the instant claims under 35 U.S.C. § 112, first paragraph on the alleged basis that successful results in the gold standard animal model for Type 1 diabetes do not necessarily translate to humans or other species. Applicants have taught the public that the claimed soluble IgGAD2 construct can prevent or delay onset of Type 1 diabetes in a standard experimental animal and have thus made a significant and useful contribution to the art, even though it could eventually be determined that the compound is without value in the treatment of humans. These data demonstrate that the claimed invention was enabled when filed. MPEP 2164.05 and *In re Brana*, 51 F.3d 1560 (Fed. Cir. 1995).

For at least these reasons, no *prima facie* case of lack of enablement has been established. Even if a *prima facie* case of lack of enablement is deemed to have been established, which is not admitted, Applicants have rebutted it. Reversal of this rejection is therefore respectfully requested.

II. Rejection under 35 U.S.C. § 103(a).

Claims 1, 2, 4, 5, 7, 13, 15 – 19, 22 – 24, and 28 – 30 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over WO 98/30706 in view of Kaufman et al., J. Clin. Invest., vol. 89, pp. 283-292 (1992) ("Kaufman"). Applicants respectfully traverse this rejection.

To establish a *prima facie* case of obviousness under 35 U.S.C. § 103, the Office must articulate a reason or rationale that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does. See, *e.g.*, *KSR* 550 U.S. 398 (2007); *Omegaflex, Inc. v. Parker-Hannifin Corp.*, 243 Fed. App'x. 592, 595-596 (Fed. Cir. 2007) citing *KSR*. Further, the Supreme Court in *KSR* also stated that "a court *must* ask whether the improvement is more than the predictable use of prior art elements according to their established functions." *KSR* at 1740; emphasis added.

Where the rationale used by the PTO to reject claims as obvious is based on some alleged teaching, suggestion, or motivation in the prior art that would have led one of ordinary skilled in the art to modify the prior art reference or to combine prior art reference teachings to arrive at the claimed invention, the PTO must articulate the following:

(1) a finding that there was some teaching suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings;

(2) a finding that there was a reasonable expectation of success; and

(3) whatever additional findings based on the Graham factual inquiries may be necessary in view of the facts to explain a conclusion of obviousness. See MPEP 2143(G).

It is further settled law that teaching away of prior art is a strong indication of nonobviousness. See *e.g. In re Soni*, 54 F.3d 746 (Fed. Cir. 1995). A prior art reference may be considered to teach away when a person of ordinary skill, upon reading the reference would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the Applicant. *Monarch Knitting Machinery Corp. v. Fukuhara Industrial Trading Co., Ltd.*, 139 F.3d 1009 (Fed. Cir. 1998).

According to the Office Action dated April 15, 2010, WO 98/30706 teaches the treatment of autoimmune disorders employing a humanized IgG2b chimeric protein wherein an autoantigen peptide is inserted into the D segment of a CDR3 loop. WO 98/30706 is silent as to GAD65, GAD1 and GAD2. Kaufman, on the other hand, is cited for its disclosure that GAD65 and GAD67 proteins may be involved in Type 1 diabetes via molecular mimicry with the coxsackievirus. Kaufman does not disclose the GAD2 peptide. The Examiner states that the full length GAD65 was one of the few known IDDM autoantigens at the time of the invention and apparently on this basis concludes that it would have been obvious to insert the full length GAD65 protein into a construct of WO 98/30706 and that such a person would have had a reasonable expectation of preventing or delaying the onset of Type 1 diabetes as of the priority date of the instant application. As such, the instant obviousness rejection is based on a "teaching, suggestion, or motivation" rationale. So the PTO's argument goes, since GAD65 was a known Type 1 diabetes autoantigen at the time of filing, one of skill in the art would have been motivated to insert it into the construct of WO 98/30706 and would have had a reasonable expectation of preventing or delaying the onset of Type 1 diabetes.

A. Erroneous Claim Interpretation.

The propriety of the instant obviousness rejection lies at least in part on the interpretation of the claim language. To properly interpret claim language, the Federal Circuit has held that

claims must be read in view of the specification of which they are a part. *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 979 (Fed. Cir. 1995). Moreover, intrinsic evidence in the form of the patent specification should guide claim construction. Along these lines, the Federal Circuit recently reinforced the importance of the specification when interpreting claim language:

> [t]he claims, of course, do not stand alone. Rather, they are part of "a fully integrated written instrument," *Markman*, 52 F.3d at 978, consisting principally of a specification that concludes with the claims. For that reason, claims "must be read in view of the specification, of which they are a part." *Id.* at 979. As we stated in *Vitronics*, the specification "is always highly relevant to the claim construction analysis. Usually, it is dispositive; *it is the single best guide to the meaning of a disputed term.*"

Phillips v. AWH Corp., 415 F.3d 1303, 1315 (Fed. Cir. 2005) (emphasis added).

Regarding claims 1-5, 7, 13, 15-19 and 22-26, the Examiner has interpreted the phrase "at least one protein fragment or peptide inserted within the variable region; wherein (a) the protein fragment or peptide is GAD2 represented by SEQ. ID NO 4..." to read on the full length, 585 amino acid GAD65 protein being inserted within the variable region. Not only is this interpretation directly contrary to the plain meaning, it is also unreasonable in view of the teachings of the specification and knowledge of a person of ordinary skill in the art and contrary to Federal Circuit case law.

First, the plain language of the claim itself specifies that "a **protein fragment** or **peptide**" is inserted in the variable region; the claim language goes on to specify that the protein fragment or peptide is GAD2 represented by SEQ. ID No. 4. The Examiner appears to impute the open transition language "comprising" onto the "protein fragment or peptide" element thereby interpreting this element as reading on a full length protein that includes the SEQ. ID No. 4 peptide. This interpretation completely ignores the fact that the claim language specifies that "a protein fragment or peptide"—not a full length protein—is inserted in the variable region. Therefore, while the open transition language may not foreclose the possibility of the recited "protein fragment or peptide" containing some additional, unrecited amino acids, the plain language specifically calling for "a protein fragment or peptide" certainly does not read on a full length protein being inserted.

The Examiner's interpretation is also inconsistent with the specification, the entire disclosure and working examples of which describe protein fragments and peptides (but not full

length proteins) inserted into variable regions. See for example page 5, lines 15 – 23, page 8, lines 1 – 11, page 9, lines 3 – 5 and 11 – 18, etc.

Furthermore, in *Genentech, Inc. v. Chiron Corp.* 112 F. 3d 495 (Fed. Cir. 1997), the court noted that "'[c]omprising' is a term of art used in claim language which means that the named elements are essential, but other elements may be added and still form a construct within the scope of the claim" (emphasis added). The Examiner's interpretation runs completely contrary to *Genentech* since it would **replace** the named claim element "a protein fragment or peptide" with an entirely different claim element—a full length protein. Again, *Genentech* stands for the proposition that the recited elements—in this case "a protein fragment or peptide"—are **essential** and thus cannot be replaced with a different element as proposed by the Examiner. While other elements may be added, no case law supports a proposition that the word "comprising" can be used to completely transform an expressly recited claim element (a protein fragment or peptide) into an altogether different element (a full length protein). In fact, *Moleculon Research Corp. v. CBS, Inc.*, 793 F.2d 1261, 1271, 229 U.S.P.Q. (BNA) 805, 812 (Fed. Cir. 1986) expressly prohibits this. The court in *Moleculon* acknowledged that "a transitional term such as 'comprising'...does not exclude additional unrecited elements, or steps (in the case of a method claim)," 793 F.2d at 1271, 229 U.S.P.Q. (BNA) at 812, but made clear that a "comprising" transition does not alter the scope of the particular claim step at issue.

> The transitional phrase, which joins the preamble of a claim with the body of a claim, is a term of art and as such affects the legal scope of a claim. While a transitional term such as "comprising" or, as in the present case, "which comprises," does not exclude additional unrecited elements, or steps (in the case of a method claim), we conclude that the transitional phrase does not, in the present case, affect the scope of the particular structure recited within the method claim's step.

For at least the foregoing reasons, the claims as properly construed do not read on the full length GAD65 protein being inserted into the variable region.

B. No rationale provided to select "a protein fragment or peptide" comprising SEQ. ID No. 4 to arrive at the claimed invention.

The Office Action provides no rationale as to why one of skill in the art would have selected SEQ. ID No. 4 from *Kaufman*'s disclosure of GAD65 and GAD67 as the protein fragment or peptide for insertion into the construct of WO98/30706. Instead, the Office Action

dated April 15, 2010 states that "[o]ne of ordinary skill in the art at the time the invention was made would have been motivated to select GAD65 as the autoantigen for use in the claimed method given the teachings of Kaufman et al. that GAD65 [the full length protein] was one of the few known IDDM autoantigens at the time of the invention." As addressed above, even if the full length GAD65 protein was one of the few known diabetic auto-antigens at the time the instant application was filed, which is not admitted and which has not been properly noticed in the record, *Kaufman* still provides no rationale to select a protein fragment or peptide comprising SEQ ID No. 4 as claimed from the virtually unlimited number of protein fragments or peptides that could be formed from the full length 585 amino acid GAD65 protein. In fact, *Kaufman* is completely silent as to SEQ ID No. 4. Absent such an articulated rationale, no *prima facie* case has been established.

C. *Kaufman* teaches away.

Not only does *Kaufman* provide no motivation to the person of ordinary skill in the art to select a protein fragment or peptide comprising SEQ. ID No. 4, *Kaufman* in fact teaches away from this peptide. *Kaufman* reports results of an epitope recognition experiment to determine the ability of sera from four diabetic subjects to recognize three polypeptide segments of GAD65. Each subject was at a different stage of disease as follows: Subject 052 (high risk), Subject 723 (patient who subsequently developed IDDM); Subject 705 (at diagnosis), and Subject UC72 (advanced neuropathy). The 3 different polypeptide segments of GAD65 tested in *Kaufman* were as follows: (A) amino acids 1 – 224; (B) amino acids 224 – 398, and (C) amino acids 398 – 585. As shown in *Kaufman*'s Figure 5, inserted below for convenience, none of the four sera reacted with polypeptide (A) (which segment SEQ. ID No. 4 falls within). On the other hand, sera from two individuals reacted with both polypeptides (B) and (C) while sera from one individual reacted with only polypeptide (C).

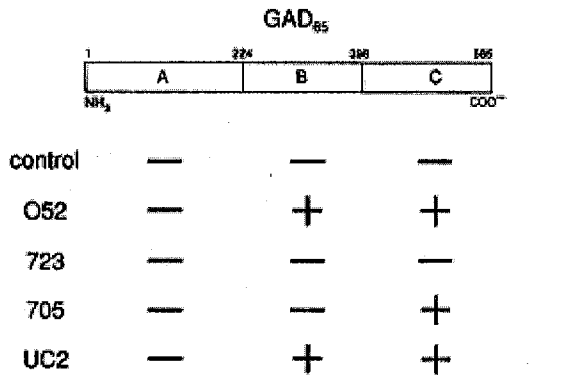

Figure 5. Epitope mapping of GAD_{65}. Three labeled segments containing the amino-terminal (*A*), middle (*B*), and carboxy-terminal (*C*) portions of GAD_{65} were immunoprecipitated with four IDDM sera that were initially characterized in the experiment shown in Fig. 4.

Since no epitopes within amino acids 1 – 224 of GAD65 were recognized by sera from IDDM patients at any stage of disease, *Kaufman*'s epitope recognition results suggest that no diabetogenic epitopes exist within this segment—the same segment in which SEQ ID No. 4 is found. Based on these results, one of skill in the art reading *Kaufman* at the time the instant invention was made would have been led away from combining a protein fragment or peptide comprising SEQ. ID No. 4 with a construct of WO 98/30706.

Because no rationale has been provided to combine Kaufman and WO 98/30706 to arrive at the claimed invention when properly construed and, in fact, *Kaufman* teaches away from such a combination, Applicants respectfully submit that no *prima facie* case of obviousness has been established. Reversal of this rejection is respectfully requested.

D. No Reasonable Expectation of Success.

The prior art can only be modified or combined to reject claims as *prima facie* obvious under a "teaching, suggestion, motivation" rationale if there is a reasonable expectation of success. MPEP 2143.02I. and *In re Merck & Co., Inc.*, 800 F.2d 1091, 231 U.S.P.Q. 375 (Fed. Cir. 1986). Even if one of skill in the art had motivation to select a protein fragment or peptide for combination with a construct of WO 98/30706, which is denied, one of skill in the art would not have had a reasonable expectation of success in preventing or delaying Type 1 diabetes. Again, because the epitope recognition studies in *Kaufman* indicated that no diabetogenic epitopes are found in amino acids 1 – 224 of GAD65, a person of ordinary skill in the art would

not have had a reasonable expectation that an epitope from that region (when used in the claimed construct) would effectively prevent or delay onset of Type 1 diabetes.

For at least the foregoing reasons, no *prima facie* case of obviousness has been established and reversal of the instant obviousness rejection is respectfully requested.

III. Rejection Under 35 U.S.C. § 112, first paragraph – Written Description Rejection.

Claims 1 – 5, 7, 13, 15 – 19, and 22 – 30 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor had possession of the claimed invention at the time the application was filed. On page 9, the Office Action states that the specification and originally filed claims do not provide support for the invention as now claimed, specifically: (A) a method comprising administration of an immunoglobulin construct comprising a protein represented by SEQ. ID NO 4 (claims 1 and 13); and (B) a method comprising the administration of an immunoglobulin construct comprising a peptide consisting of amino acid residues 206-220 of GAD65 (claim 26). Applicants respectfully traverse this rejection.

Claims 1 and 13 each claim a method of preventing or delaying onset of Type 1 diabetes comprising, *inter alia*, administering to a subject a soluble fusion protein comprising at least one immunoglobulin having at least one protein fragment or peptide inserted in the variable region, wherein the protein fragment or peptide is (claim 1), or consists essentially of (claim 13), GAD2 represented by SEQ. ID NO 4. Claim 26 claims the method of claim 13 wherein the at least one protein fragment or peptide consists of amino acid residues 206-220 of GAD65. Amino acid residues 206-220 of GAD65 correspond to the sequence listing filed on February 9, 2007, and appearing in the specification as filed on pages 45-46: Thr-Tyr-Glu-Ile-Ala-Pro-Val-Phe-Val-Leu-Leu-Glu-Tyr-Val-Thr (or TYEIAPVFVLLEYVT).

As an initial matter, claims 1 and 13 do not specify "a protein represented by SEQ. ID. No. 4." Instead, claim 1 specifies that the construct has "at least one protein fragment or peptide inserted within the variable region; wherein (a) the protein fragment or peptide is GAD2 represented by SEQ. ID NO 4." As such, the rejection is facially deficient and no *prima facie* case of lack of written description has been established.

Even though no *prima facie* case of lack of written description has been established, Applicants point out that the specification as filed fully supports the claimed subject matter for at least the following reasons.

On page 3 of the Office Action mailed on August 24, 2007, the Examiner stated: "There is insufficient written description to show that Applicant was in possession of a 'protein fragment or peptide derived from GAD', ***except for GAD65 peptides 524-543 and 206-220***" (emphasis added). Therefore the Examiner has already acknowledged that the specification adequately shows that Applicants had possession of a protein fragment or peptide derived from GAD65 identical to GAD2, also referred to as SEQ. ID NO 4.

In addition, Applicants note that the specification as filed is replete with written support for an immunoglobulin construct comprising a protein represented by GAD2/SEQ. ID NO 4/GAD65 residues 206-220. GAD2 is identified as SEQ. ID NO 4 on pages 45-46 of the specification as filed, and further defines GAD2/SEQ. ID NO 4 as corresponding to amino acid residues 206-220 of GAD65 (Thr-Tyr-Glu-Ile-Ala-Pro-Val-Phe-Val-Leu-Leu-Glu-Tyr-Val-Thr or TYEIAPVFVLLEYVT). *See also* Sequence Listings filed on February 9, 2007, in response to the Office Communication mailed January 19, 2007, requesting initial CRF and paper copies of the Sequence Listing.

Furthermore, the specification as filed contains multiple descriptions of an immunoglobulin construct comprising GAD2/SEQ. ID NO 4. For example and without limitation:

- "The present invention is also directed to a methods, kits, combinations, and compositions, comprising: a pharmaceutically-effective amount of an immunoglobulin, or portion thereof, linked to a protein fragment or peptide, wherein the immunoglobulin, or portion thereof, can bind to an Fc receptor. Illustratively, the peptide comprises INSβ, GAD 1, or GAD2." Page 19, lines 1-5.

- "In yet another embodiment of the present invention, the immunoglobulin comprises Ig-INSβ, Ig-GAD1, Ig-GAD2, or an immunoglobulin, or a portion thereof, linked to a peptide, for example a peptide derived from GAD65 or an insulin protein." Page 22, lines 3-5.

- "In yet another embodiment of the present invention, the composition comprises IgINS (peptides derived from human insulin), IgGAD (peptides derived from GAD), IgINSβ, IgGAD1 and IgGAD2." Page 23, lines 2-4.

- "In one embodiment of the present invention, the composition comprises Ig-INSβ, Ig-GAD1, IgGAD2 or an immunoglobulin or a portion thereof linked to a peptide derived from GAD65." Page 24, lines 6-8.

- "In one embodiment of the present invention, a composition is provided comprising an immunoglobulin or portion thereof linked to a protein fragment or peptide wherein the immunoglobulin or portion thereof is capable of binding to an Fc receptor, the peptide being selected from the group consisting of peptides derived from INS and GAD and more specifically INSβ, GAD 1 and GAD2, the composition having the property of being endocytosed by cells bearing the Fc receptor and processed and presented by the cells to present the peptide to endogenous MHC Class II molecules, thereby substantially reducing or preventing activation of diabetogenic T cells specific for the peptide." Page 24, lines 14-21.

- "Other peptides that may be inserted within the variable region within the CDR region of an Ig and utilized for creating compositions for the treatment of type 1 diabetes as taught in the present invention are: GAD1 (Glutamic acid decarboxylase-65 also known as 'GAD65'); corresponding to amino acid residues 524-543 of GAD 65 (Seq. I.D. No. 3 [SRLSKVAPVIKARMMEYGT]) to create chimera Ig-GAD1; and 2) GAD2; corresponding to amino acid residues 206-220 of GAD 65 (Seq. I.D. No. 4 [TYEIAPVFVLLEYVT]); and other peptides derived from GAD65." Page 45, line 20, to page 46, line 2 (bracketed text appears in original).

On page 9, the Office Action states that the specification "does not teach a peptide consisting of amino acid residues 206-220 of *any* GAD65, e.g., mouse GAD65, rat GAD65, horse GAD65, etc." Applicants note that the claims are to be read in light of the specification. The specification clearly defines (by chemical formula) "amino acid residues 206-220 of GAD65," as a peptide having the chemical formula set forth in SEQ. ID NO 4. Applicants again point to language at page 45, line 20, to page 46, line 2, of the specification as filed reciting: "amino acid residues 206-220 of GAD 65 (SEQ. I.D. No. 4 [TYEIAPVFVLLEYVT])" (bracketed text appears in original specification as filed). Therefore, one of skill in the art reading the specification would immediately recognize that amino acid residues 206-220 of GAD65 are referred to in the specification as SEQ. ID NO 4 which has the amino acid sequence TYEIAPVFVLLEYVT, regardless of the native source of the GAD65 protein.

For at least these reasons, a person having ordinary skill in the art at the time the application was filed would have reasonably understood that Applicants possessed an

immunoglobulin construct comprising a protein represented by SEQ. ID NO 4 and/or amino acid residues 206-220 of GAD65. Accordingly, Applicants respectfully request the withdrawal of the rejections of claims 1 – 5, 7, 13, 15 – 19 and 22 – 30 under 35 U.S.C. § 112, first paragraph.

IV. Obviousness Type Double Patenting Rejection.

Claims 1 – 5, 7, 13, 15 – 19, 22 – 25, and 27 – 30 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting over claims 1 – 7 and 13 – 16 of U.S. Serial N0. 11/290,070 and claims 1 – 7 and 13 – 16 of U.S. 11/425,084. Applicants will address these provisional rejections upon resolution of the outstanding non-provisional rejections.

CONCLUSION

The application is believed to be in condition for allowance. Early and favorable considerations is respectfully requested. The Commissioner is hereby authorized to charge deposit account 02-1818 for any fees which are due and owing.

Respectfully submitted,

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